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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,434	01/07/2002	David Wallach	WALLACH=1D	4966

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,434	WALLACH ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 24 August 2004 is acknowledged and entered. Following the amendment, claims 1-4, 6-8 and 10 are amended.

Currently, claims 1-4, 6-8 and 10 are pending and under consideration.

Declaration

The declaration under 37 CFR 1.132 filed 24 August 2004 is insufficient to overcome the prior art rejection of claims 1-4, 6-8 and 10 based upon the references by Seckinger et al. (J. Exp. Med., April 1, 1988, 167(4): 1151-6), and Dayer et al. (J. Exp. Med., 1985, 162: 2163-2168) as set forth in the last Office action for the following reasons: the declaration incorporates the details of method of purification of the protein used in the presently claimed method, indicating that the protein is, therefore, "substantially purified" (pages 2-4), and has a specific activity of about 600,000 units/mg, which is over three orders of magnitude difference in comparison to that in the prior art by Peetre cited by the examiner, and that the process of the Seckinger publication cannot obtain purification substantially better than that described by the Peetre publication (page 5). This is not persuasive because MPEP indicates that (in *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989)) while the applicant questioned the purity of the prior art factor, no concrete evidence of an unobvious difference was presented, that the Board stated that the dispositive issue is whether the claimed factor exhibits any unexpected properties compared with the factor disclosed by the prior art (MPEP 2113). Therefore, purity alone does not make a product novel or nonobvious over the prior art. With respect to the specific activity of about 600,000 units/mg, and three orders of magnitude difference, it cannot be used to support the difference or unexpected property between the protein of the prior art and that of the present application because applicants compare the data from a reference *not cited* by the examiner (the Peetre publication). Further, it is improper to compare the results between the prior art by Seckinger (cited by the examiner) and the present application because the assays were not parallel experiments, and they were carried out differently. For example, the cell types used

were different, which may result different sensitivity in the assay, and the definition of "one unit" was defined differently in the prior art and in the present application.

At page 6 of the declaration, the applicant argues that in applicants opinion, those of ordinary skill in the art at the time the Peetre and Seckinger publications were published would not have found it obvious how to obtain the substantially purified protein of the present invention with the crude preparation of Peetre and Seckinger. This is not persuasive because the methods used by applicants such as ion exchange and reversed phase HPLC and many other alternative methods have been well established long before the present invention was filed, and were notoriously known and widely practiced in the field for protein purification. It is also well known that proteins behave differently in a purification process due to their different physiochemical features. As such, choosing a particular method among well established methods, or optimizing certain parameters such as pH and ion type or concentration in a well established method for a specific protein is hardly non-obvious, and does not constitute inventive concept.

Withdrawal of Objections and Rejections:

The rejection of claims 3, 4, 7 and 8 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-8 and 10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Seckinger et al. (J. Exp. Med., April 1, 1988, 167(4): 1151-6), in view of Dayer et al. (J. Exp. Med., 1985, 162: 2163-2168), for the reasons of record set forth in the last Office Action mailed on 24 February 2004, at pages 3-4.

Applicants argument filed on 24 August 2004 has been fully considered, but is not deemed persuasive for reasons below.

At pages 11-13 of the response, the applicant argues that the present invention would not have been obvious from the combination of cited references as Seckinger does not disclose any TNF-α inhibitory factor of sufficient purity to be used therapeutically, that a prior art rejection over Seckinger in the grandparent application 08/474,691 (now US5,981,701) was avoided by specifying in the claim that it was a substantially pure protein (through a declaration), and that those of ordinary skill in the art would understand that the term "substantially purified" does not comprehend the purity obtained only by ion exchange chromatography ("partially purified"). Applicants further argue, at pages 13-15, that Seckinger only obtains partial purification, and refers to his material as "semi purified inhibitor" or "partially purified Sephadex S-200 urine", that Seckinger's purification was only a very crude protein mixture, that selecting the proper separation technique and the proper conditions within the separation techniques did not involve mere routine experimentation, and accordingly, the very substantial additional purification needed to obtain the substantially purified protein in claim 2 of the '701 patent not only differentiated the partially purified proteins of Seckinger, but also established obviousness thereover. These arguments are all based on one issue, the purity of the protein, and they are not persuasive because "mere purity of claimed compound does not render substance unobvious" (*Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). In *Ex parte Gray*, the Court cites the case law, *In re Bergstrom*, 1 57 CCPA 1240, 427 F.2d 1394, 166 USPQ 256 (1970), involving a rejection of certain pure prostaglandin compounds for not being novel in light of the material from which it was extracted, which held that the sole issue it accurately posed is

'whether the *claimed* pure materials are *novel* as compared with the *less pure* materials of the reference' [emphasis supplied.], and that "it seems to us that the answer to that question is self-evident: by definition, pure materials necessarily differ are the only ones existing and available as a standard of reference, as seems to be the situation here, perforce the 'pure' materials are 'new' with respect to them." Therefore, the term "substantially purified" is a relative term. In the instant case, besides molecular sieve chromatography using a Sephacryl S-200 column as applicants pointed out, Seckinger also purified the protein by FPLC (page 1512, the second paragraph), which is comparable to that used in the present application. Thus, the resulted product from Seckinger's FPLC cannot be considered just "a very crude protein mixture", and certainly meet the limitation of "substantially purified".

Further, in *Ex parte Gray*, the Court opinioned that "the difference between the material of Goldstein and of Walker and that claimed by appellants herein resides in the method of obtaining the human growth factor. ... the dispositive issue before us is whether the claimed factor exhibits any *unexpected properties* compared with that described by the cited publication items. In the instant case, the prior art reference by Seckinger discloses, besides the similar physiochemical features and source of isolation, the same biological property of the protein, inhibiting TNF- α, as that in the present invention regardless the alleged "less purity". There is no unexpected property disclosed in the present specification for the "substantially purified" protein used in the claimed invention in comparison to that of Seckinger's. "It is therefore entirely proper that appellants should have shouldered their burden of persuasion and made some comparison between the two materials to establish unexpected properties for the claimed factor. Having failed to do so, appellants are in a poor position now to contend that any doubt as to the difference between the two materials should be resolved in *favor* of patentability" (*Ex parte Gray).*

Furthermore, with respect to the argument that that selecting the proper separation technique and the proper conditions within the separation techniques did not involve mere routine experimentation, neither the present specification nor the declaration has shown objective evidence to establish that any method used for the purification of the protein in the present invention was unknown to those skilled in the field. In fact, the methods such as ion exchange and reversed phase HPLC have been well established long before the present invention was filed,

and were notoriously known and widely practiced in the field for protein purification. It is also well known that proteins behave differently in a purification process due to their different physiochemical features. As such, choosing a particular method among well established methods, or optimizing certain parameters such as pH and ion type or concentration in a well established method for a specific protein is hardly non-routine experimentation, and does not constitute inventive concept.

Conclusion:

No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Elizabeth C. Kemmerer

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/14/05